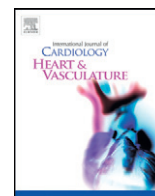




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Overweight predicts poorer exercise capacity in congenital heart disease patients☆

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ABSTRACT

Background: Overweight (OW) and obesity (OB) are endemic in the United States and affect adolescents and adults with congenital heart disease (ACHD). Defining the burden of excess weight on the cardiovascular system in ACHD is the goal of this study. Limitation of exercise capacity due to overweight or obesity might be reversible with weight loss and improve quality of life for ACHD adults.

Methods: Exercise tests performed using a Bruce protocol and measurement of maximum oxygen consumption were retrospectively reviewed on 418 CHD patients. OW and OB were defined as the 85–95 or >95 percentile respectively for age and gender or by adult criteria. Severity of CHD was assigned based on criteria published in standard guidelines.

Results: 63 patients had mild, 198 moderate, and 157 severe heart disease. Each ACHD group was 32 to 34% OW or OB. Measured exercise time (ET) of CHD patients with moderate or severe heart disease was less than that of controls in each weight categories. However, OB or OW people have shorter ET than their normal weight peers with CHD. Multiple regression using ET as the dependent variable finds that female sex, relative BMI, and VE/VCO₂ at peak exercise are all associated with lesser ET with high significance. Peak heart rate is associated with greater ET, with borderline significance. Severity of heart disease is not independently associated with ET.

Conclusions: OW and OB are strongly associated with reduced ET in persons with congenital heart disease. Losing weight may improve exercise capacity in ACHD.

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1. Introduction

The prevalence of overweight and obesity in children and adolescents in the US has increased significantly in the last three decades [1]. Overweight is defined as having excess body weight for height from fat, muscle, bone, water, or a combination of these factors [2]. Obesity is defined as having excess body fat [3]. Empirically, overweight is defined as BMI above the 85% and below the 95% for age and obesity as BMI above the 95th percentile for age.

The proportion of adolescents and adults with congenital heart disease (CHD) with overweight and obesity parallels that of the general population. Exercise restrictions or concerns about capacity to exercise in persons with CHD may lead to a higher prevalence of poor fitness. Ferns et al. demonstrated reduced exercise capacity in boys and girls who were obese compared with their peers over the age range 4 to 18

years. Obese participants had higher heart rates early in exercise than those of normal weight [4]. Higher resting heart rates have been demonstrated in children who are obese compared to their lean peers [5]. Obesity in children, as well as adults, is associated with endothelial dysfunction and multiple markers of inflammation raising concern about additional burden to people with structural heart disease [6].

The population of adolescents and adults with congenital heart disease is increasing rapidly leading to interest in evaluating morbidity associated with excess weight in this population.

2. Methods

We retrospectively examined the results of clinically indicated exercise tests obtained over a three year period, all of which utilized the Bruce treadmill protocol. We excluded individuals with pacemakers, and included 418 tests of adolescents and adults with CHD. Congenital heart disease was stratified into mild, moderate, severe using criteria in the guidelines of the American Heart Association and American College of Cardiology. Beta blockers were prescribed in 13 CO and 86 CHD patients. Patients with no structural heart disease had test indications of chest pain, arrhythmia, dyspnea, or other symptoms. Parameters extracted included maximum oxygen consumption, maximum

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exercise time (seconds), RER, maximum respiratory rate, beta blocker treatment, presence of pacemaker, maximum respiratory rate, ethnicity, gender, VE/VCO₂ at peak exercise. Patients were allocated to one of three groups based on body mass index: normal, overweight, or obese using age specific criteria for adolescents and adults.

Comparisons were made of congenital heart disease patients to controls. Differences in each parameter between groups were assessed by non-parametric analysis and t test of means.

Using maximum exercise time as a dependent variable, multiple logistic regression analyses were made including cases and controls in the dataset and the independent variables sex, age, VE/VCO₂ at peak exercise, pre-exercise systolic blood pressure, relative BMI, severity of heart disease, and maximum heart rate. Additional analysis was made for the dependent variable VE/VCO₂ at peak exercise. Median RER was 1.1 (SD 0.1) for both cases and controls indicating good exercise effort during testing.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the human research committee at Children's National Medical Center.

3. Results

3.1. Demographics

The distribution of cases in the study sample is outlined in Table 1. The study sample included exercise tests of 418 patients with congenital heart disease (CHD). Distribution of weight as normal, overweight, or obese was similar in the two groups. Demographic variables BMI range, beta blocker usage, severity of heart disease, VE/VCO₂, and BNP are all highly correlated.

3.2. Exercise time

Cases that were of normal weight exercised longer than cases that were overweight or obese. Table 2 shows maximum ET for CHD stratified both by relative body mass index and by severity of heart disease.

ET is associated with relative body mass index for all patients stratified by severity of heart disease; mild, moderate or severe. As expected maximum oxygen consumption shows the same association; peak

Table 1
Population characteristics.

Parameter	Congenital heart disease N (%)
Male	214 (51)
Female	204 (49)
Race	
White	282 (67)
African American	96 (23)
Hispanic	17 (4)
Asian	5 (1)
Not specified	18 (4)
Heart defect severity	
Mild	63 (15)
Moderate	198 (47)
Severe	157 (38)
BMI range	
0–85%	260 (67)
85–95%	78 (19)
95–100%	60 (14)
Continuous	Mean (SD)
Age	24.3 (8.5)
BMI	24.5 (5.3)
Weight (kg)	70.5 (16.3)
Height (cm)	169.6 (10.3)

418 people comprised the study population, of whom 19% were overweight and 14% obese.

Table 2
Exercise parameters stratified by relative body mass index and severity of heart disease.

Severity	BMI	No	Variable	Case Mean (SD)
Mild	Normal	43	Max ET	565.6 (176.6)*
			Max HR	180.5 (13.9)*
			Max VO ₂	38.8 (9.5)*
	OW	15	Max ET	418.7 (141.6)
			Max HR	157.1 (20.3)
			Max VO ₂	28.1 (7.5)
	OB	5	Max ET	357.0 (153.1)
			Max HR	164.6 (18.3)
			Max VO ₂	23.7 (7.0)
Moderate	N	131	Max ET	459.4 (154.9)*
			Max HR	161.7 (24.6)
			Max VO ₂	29.9 (8.4)*
	OW	34	Max ET	422.7 (140.2)
			Max HR	161.7 (24.6)
			Max VO ₂	26.8 (7.2)
	OB	33	Max ET	367.0 (140.2)
			Max HR	158.7 (20.2)
			Max VO ₂	23.8 (8.2)
Severe	N	106	Max ET	464.7 (141.6)*
			Max HR	154.7 (30.3)
			Max VO ₂	27.8 (7.4)*
	OW	29	Max ET	381.2 (140.2)
			Max HR	160.4 (20.2)
			Max VO ₂	24.8 (5.9)
	OB	22	Max ET	326.6 (114.2)
			Max HR	150.4 (25.6)
			Max VO ₂	19.6 (4.7)

By ANOVA maximum exercise time and VO₂ max are significantly different for increasing BMI categories in each category of severity of heart disease, marked by *. Maximum heart rate is associated with increasing BMI only in patients with mild heart disease.

heart rate is not associated with degree of overweight in patients with moderate or severe disease. Obese patients have shorter ET than overweight patients or patients of normal weight with the same severity of heart disease. Within the group of patients with severe heart disease, for example, maximum exercise time was 462.9 s for normal weight patients, 381.2 s for overweight patients, and 326.6 s for obese patients, a loss of 136.3 s or 29% of the exercise time of patients with severe heart disease and normal weight.

When patients are stratified by relative BMI, only in patients of normal weight are maximum exercise time, maximum oxygen consumption, and maximum heart rate associated significantly with severity of heart disease. In patients with obesity or overweight maximum exercise time and maximum heart rate are not associated with severity of heart disease; the association of VO₂ with severity persists with moderate significance (P0.027).

Males exercised longer than females in CHD cases and controls across the range of disease severity. In males with mild or moderate disease, maximum heart rate was significantly higher than in females but this difference was absent in controls or cases with severe disease.

3.3. Blood pressure

Subjects had significantly increased pre-exercise systolic and diastolic blood pressure with increasing body mass category as shown in Table 3. Post-exercise systolic and diastolic blood pressures also were significantly higher in subjects with OW or OB compared to those of normal weight across categories of gender or severity of heart disease. The higher post-exercise blood pressures do not represent greater exercise effort since, in fact, overweight and obese patients had shorter exercise times. See Table 3.

3.4. Association of exercise time to independent variable

Using multiple regression, we analyzed ET as a dependent variable to gender, age, VE/VCO₂ at peak exercise, pre-exercise systolic blood

Table 3

Blood pressure pre- and post-exercise stratified by relative body mass index.

Group		Normal weight	Overweight	Obese	Significance by non-parametric testing
CHD before ETT	Systolic BP	105.73 (12.04)	106.86 (15.73)	112.72 (8.67)	0.0001
CHD before ETT	Diastolic BP	63.25 (6.51)	65.85 (6.76)	70.49 (7.07)	0.0001

Resting systolic and diastolic blood pressure are higher in persons who are overweight or obese.

pressure, relative BMI, severity of heart disease, and maximum heart rate achieved. Data is shown in Table 4. Female gender but not age was associated with shorter ET. Severity of heart disease was not a predictor of maximum ET but relative BMI was a strong predictor as was VE/VCO₂ at peak exercise. For each increment in relative BMI, e.g. normal weight to overweight or overweight to obese, maximum ET fell by 69.8 s.

3.5. Ventilatory equivalent

VE/VCO₂ at peak exercise was strongly associated with exercise time (Table 5). We analyzed VE/VCO₂ at peak exercise as a dependent variable with the same group of independent variables including maximum ET. VE/VCO₂ did not vary with gender. We did not have the capacity to measure VE/VCO₂ slope but others have shown correlation of the measurement at peak exercise with outcomes in heart failure [7,8]. VE/VCO₂ at peak exercise is associated with maximum heart rate achieved, severity of heart disease, and, with weak impact, with relative overweight or obesity, consistent with VE/VCO₂'s association with heart function or heart failure.

4. Discussion

Obesity is a serious health problem in the United States. NHANES data from 2009–2010 shows a 16.9% prevalence of obesity in children age 2 to 19 years, with a relatively stable prevalence since the 1980s [9]. The impact of this on the emerging population of adults with congenital heart disease has not been systematically addressed.

Obesity in children with CHD is as prevalent as obesity in the general population. Concern has been raised about whether children and adults with CHD are counseled to avoid or limit sports participation and whether this might impact their fitness and weight. In one study children with CHD who are exercise restricted have a higher prevalence of obesity than children not so restricted [10]. Dua measured exercise over two periods of normal life style in adults with CHD at three levels of severity. Adults did not reach British guidelines for physical activity in any group; however, more symptomatic adults had lower levels of physical activity than less symptomatic adults despite an expressed interest in greater fitness. These authors did not find a correlation of fitness with overweight or obesity [11].

Relative overweight and obesity are strongly correlated with decreased exercise capacity such that obesity is associated with a 27% reduction in exercise time in ACHD. Among obese or overweight patients with CHD, exercise time does not vary with severity of heart

disease. This suggests that obesity is a significant factor in short ET. It is not clear what the interaction is of fitness with relative overweight in these findings; less fit patients may be more overweight because of lack of caloric expenditure. However, the reduction in exercise time in OW or OB CHD even with less severe heart disease is striking.

The finding of elevated mean arterial pressure in a youth population in which 11.7% of the population was obese is also noted in a study of presumed healthy children by Ferns et al. They found that fitness moderates the association of elevated arterial pressure with body mass index. In their data OB boys exercised for 114 s less and OB girls for 91 s less than their peers of normal or OW status. We found that males had longer exercise times than females, as did Serratto et al.

OB has systemic effects on the body including effects on the endothelium which are of particular concern in individuals with CHD. Inflammatory mediators associated with adult atherosclerosis and with insulin resistance were demonstrated in obese children by Schipper et al. [12] Concern about this led to the formation of an NHLBI working group and recommendations in 2010 [13]. In our study systematically collected data about lipid profile, inflammatory mediators, insulin resistance, or endothelial function were not available. However, pre-exercise systolic or diastolic blood pressures, while normal, are significantly higher in cases with OW or OB than in the normal weight individuals. In a study of English school children, exercise fitness moderated the effect of OB on elevated blood pressure, suggesting that fitness even without weight change may benefit long term cardiovascular risk [14].

4.1. Study Limitations

This is a retrospective study of a convenience cohort of individuals referred from our program for exercise testing. Exercise tests were not evaluated sequentially as a function of weight change, something that would be of interest in a future study.

5. Conclusions

A most relevant question not answered by our observations is whether or not improved fitness and or weight loss in adolescents or young adults with CHD will improve exercise capacity and/or endothelial function. Measured peak oxygen consumption in adults with frequent physical activity improved over time compared with those who were sedentary [15]. In a randomized controlled trial of exercise

Table 4Regression of maximum exercise time to independent variables. The model is significant with adjusted R square of 0.2984. Variables predictive of maximum exercise time include sex, peak VE/VCO₂, relative BMI and maximum heart rate.

Variable	Df	Estimate	S.E.	B	P	5% CI	95% CI
Intercept	1	615.28	93.06	6.61	0.0001	432.29	798.27
Sex	1	−57.89	13.09	−4.42	0.0001	−83.63	−32.15
Peak VE/VCO ₂	1	−5.00	1.16	−3.96	0.0001	−7.48	−2.52
Relative BMI	1	−69.86	879	−7.94	0.0001	−87.15	−52.57
Severity	1	1.08	9.51	0.11	0.91		
Pre-ETT systolic BP	1	−0.35	0.52	−0.68	0.50		
Maximum HR	1	1.37	0.28	4.87	0.0001	0.82	1.92

Table 5Regression of VE/VCO₂ at peak exercise to independent variables. The model is significant with adjusted R square of 0.2569. Variables predictive of maximum exercise time include sex, peak VE/VCO₂, relative BMI and maximum heart rate. Beta blocker therapy was not significantly associated with VE/VCO₂. The association with relative BMI is statistically significant but has less power than its association with maximum ET.

Variable	Df	Estimate	S.E.	B	P	5% CI	95% CI
Intercept	1	43.09	2.42	17.84	<0.001	38.35	47.84
Severity	1	2.63	0.18	8.84	<0.001	1.27	2.00
BMI	1	−0.20	0.04	−5.00	<0.001	−0.28	−0.12
Max HR	1	−0.04	0.01	−3.78	0.0002	−0.06	−0.02
Max ET	1	−0.01	0.00	−4.77	<0.001	−0.01	−0.00

training in adolescents with congenital heart disease, a structured exercise program increased maximum oxygen consumption at testing and doubled the number of participants reporting moderate to vigorous physical activity at home [16]. Counsel from cardiologists to encourage exercise and maintenance of healthy weight should be part of the care of the child, adolescent and adult with congenital heart disease. Reassurance that some shortness of breath and fatigue are expected with exercise may assist the child or adult to continue to exercise and to lose weight.

Conflict of interest

No conflict of interest exists for any author.

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